REMARKS

The Office Action mailed October 28, 2002 has been carefully reviewed and the following remarks are made in response thereto.

In view of the foregoing amendment and the following remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

The amendments to claims 1 and 2 are supported, for example, in the specification at page 4, lines 15-34. The amendments to claim 3, 4, 6-11, 13. 15 and 16 are clarifications of the Markush groupings and are supported by the sequence listing. Support for the amendment to claim 11 is found, for example, at page 4, line 35 to page 5, line 12. Amendments to claims 11-16 have been made to remove language deemed objectionable by the Examiner but do not affect the scope or substance of the claim. Claim 21 has been canceled without prejudice or disclaimer, the subject matter thereof having been incorporated into now independent claim 2. Applicants respectfully submit that no prohibited new matter has been introduced by the amendment.

I. Summary of the Office Action

1. The Office Action objected to the specification for the recitation of a URL at page 8, line 18.

2. The Office Action rejected claims 1, 2 and 21 under 35 U.S.C. §112, 1st paragraph, alleging that the inventors did not have possession of the claimed invention.

3. The Office Action rejected claims 3-16 under 35 U.S.C. §112, 2nd paragraph for being indefinite in the form of reciting Markush groups.

4. The Office Action rejected claim 11 under 35 U.S.C. §112, 2nd paragraph for being indefinite in reciting "sequence specific probe."

5. The Office Action rejected claims 11-16 under 35 U.S.C. §112, 2nd paragraph for being indefinite in the recitation of "the segment includes at least 20 bases...which differ."

6. The Office Action indicated the allowability of claims 3-10 if the 35 U.S.C. §112, 2nd paragraph rejections pertaining thereto are corrected.

II. Response to the Office Action

At the outset, Applicants note with appreciation the Examiner's indication that claims 3-10 are free of the prior art.

Objection to the specification

The Office Action objected to the specification for containing a URL at line 18 of page 8, alleging that the recitation of the naked URL may still be a hyperlink in some "word processing programs." While Applicants believe that the new objection is erroneous in the interpretation of the policy set forth in MPEP 608.1, in order to avoid needless delays in prosecution the specification has again been amended, placing a space within the URL and directing the user to remove the space. Accordingly, Applicants respectfully request withdrawal of the ground of objection.

Rejection of claims 1, 2 and 21 under 35 U.S.C. §112, 1st paragraph as lacking sufficient written description

The Office Action contends that there is insufficient written support in the specification for claims drawn to isolated nucleic acid molecules "comprising" at least 100 contiguous bases of a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 2, 3, 4, 5, 6, 8, 9 and 10 (claim 1) or comprising an entire sequence of SEQ ID NOs: 2-10 (claims 2 and 21). The Office Action relies upon a reference published after the filing date to which the instant application is entitled that discloses an *M. tuberculosis* sequence of 3,534 bases to allege that there is "expected" variation among the species of DNA which encode the mycobacterial rpoB gene. In accordance with the Examiner's suggestion, Applicants have amended claims 1 and 2 to recite "consisting of" rather than "comprising" in order to clearly convey the nature of the rpoB sequences. Accordingly, Applicants respectfully request withdrawal of the ground of rejection.

Rejection of claims 3-16 under 35 U.S.C. §112, 2nd paragraph for being indefinite

The Office Action contends that the claims are indefinite in the recitation of a Markush group in the form of "selected from the group consisting of SEQ ID NOS: 2-10." The Office Action asserts that a Markush group must contain the word "and." It is respectfully submitted that this is a misinterpretation of the ruling, whose intent is to sanction

claims to "a genus expressed as a group consisting of certain specified materials." MPEP 2173.05(h). The recitation of "2-10" when referring to sequences disclosed in an application is 'closed language' and represents no more ambiguity or uncertainty than the recitation of "2, 3, 4, 5, 6, 7, 8, 9 and 10" to represent the exact same genus. Nonetheless, the claims have been so amended and Applicants respectfully request withdrawal of the ground of rejection.

The Office Action further contends that claim 11 is indefinite in the recitation of "sequence specific probe," stating that it cannot be determined what limitation the phrase brings to the claim. Applicants respectfully point out that under the statute Applicant can be his own lexicographer. In the ground of rejection, it is clear that the meaning of the term is clearly understood in the context of the claim by the Examiner. Accordingly, the term is not being used in a manner which is repugnant to its art accepted meaning and is proper. Applicants have, however, amended the claims to recite the term "polynucleotide" and respectfully request withdrawal of the ground of rejection.

The Office Action further contends that claims 11-16 are indefinite in the recitation of "the segment includes at least 20 bases...which differ..." in claim 11. In response, claim 11 has been amended to state that the "segment of the mycobacterial rpoB sequence" to which the sequence-specific probe hybridizes is a contiguous segment and comprises at least about 5 nucleotide bases of SEQ ID NO: 2, 3, 4, 5, 6, 8, 9, or 10 that are different from the corresponding at least about 5 nucleotide bases of SEQ ID NO: 1 when the sequences are maximally aligned. Accordingly, Applicants respectfully request withdrawal of the ground of rejection.

Rejection of claims 11-15 under 35 U.S.C. §102(b) as being anticipated by DeBeenhouwer et al (WO 95/33851)

The Office Action alleges that the claims are anticipated by DeBeenhouwer because the reference teaches rpoB sequences which are identical to SEQ ID NOs: 2-10 of the present invention over at least about 20 nucleotide bases and have nucleotide base differences from the *M. tuberculosis* rpoB sequence SEQ ID NO: 1. The Office Action particularly points out a nucleic acid sequence, MA-POL-1, disclosed by DeBeenhouwer which is complementary to SEQ ID NO: 7 over bases 41-63 of SEQ ID NO: 7, but differs from SEQ ID NO: 1 at positions 47, 50, 53, 56 and 59. Applicants respectfully traverse the ground of rejection as applied to the claims as amended herewith. Claim 11 has been amended to delete reference

to SEQ ID NO: 7 and to more clearly point out that the polynucleotide comprises at least about 5 nucleotide bases which are identical to the corresponding bases in the contiguous segment of SEQ ID NO: 2-10 to which the polynucleotide hybridizes under stringent conditions with the *proviso* that those at least about 5 bases are different from the corresponding bases of SEQ ID NO: 1 when the sequences are maximally aligned. While the disclosure of DeBeenhouwer comprises sequences containing regions which are identical to a corresponding contiguous segment of the claimed SEQ ID NOs: 8 and 10 which comprises some differences from SEQ ID NO: 1, none of those sequences disclosed by DeBeenhouwer comprise at least 5 bases that are different from SEQ ID NO: 1 when the sequences are maximally aligned. In order to satisfy the metes and bounds of the present invention as claimed, the segment must contain at least 5 bases of SEQ ID NO: 2, 3, 4, 5, 6, 8, 9 or 10 that are different from SEQ ID NO: 1, and the DeBeenhouwer reference clearly falls short in this regard. Accordingly, DeBeenhouwer cannot be interpreted as an anticipatory reference and Applicants respectfully request withdrawal of the ground of rejection.

Conclusion

In view of the foregoing amendments and remarks, the Applicants respectfully request withdrawal of all outstanding rejections and early notice of allowance to that effect.

EXCEPT for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. § 1.136(a)(3).

If the Examiner finds that a telephone conference would further prosecution of this application, the Examiner is encouraged to call the undersigned.

Respectfully submitted,
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APPENDIX

Marked-Up Copy of Amendments to Specification and Claims

Added Text

[~~Deleted Text~~]

IN THE SPECIFICATION:

Please replace the paragraph beginning at page 8, line 12 and ending at page 9, line 11 with the following:

-- One example of algorithm that is suitable for determining percent sequence identity and sequence similarity is the BLAST algorithm, which is described in Altschul *et al., J. Mol. Biol.* 215:403-410 (1990). Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information (~~www.ncbi.nlm.nih.gov~~ www.ncbi.nlm.nih. gov – without the space before "gov"). This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short words of length W in the query sequence, which either match or satisfy some positive valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul *et al., supra*). These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing them. The word hits are then extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Cumulative scores are calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always > 0) and N (penalty score for mismatching residues; always < 0). For amino acid sequences, a scoring matrix is used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T, and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, and expectation (E) of 10, a cutoff of 100, M=5, N=-4, and a comparison of both strands. For amino acid sequences, the BLAST P program uses as defaults a wordlength (W) of 3, an expectation (E) of 10, and the BLOSUM62 scoring matrix (*see* Henikoff & Henikoff (1989) Proc. Natl. Acad. Sci. USA 89:10915).--

IN THE CLAIMS:

1. (Five Times Amended) An isolated rpoB nucleic acid molecule [~~comprising~~] consisting of at least about 100 contiguous bases of a sequence selected from the group consisting of SEQ ID NOS: 2, 3, 4, 5, 6, 8, 9 and 10 [~~from a rpoB sequence selected from the group consisting of SEQ ID NOS: 2, 3, 4, 5, 6, 8, 9 and 10~~].

2. (Five Times Amended) [The] An isolated nucleic acid molecule [of claim 1 comprising] consisting of a rpoB sequence selected from the group consisting of SEQ ID NOS: 2, 3, 4, 5, 6, 7, 8, 9 and 10.

3. (Five Times Amended) A probe which is the complement of a rpoB sequence selected from the group consisting of SEQ ID NOS: [~~2-10~~] 2, 3, 4, 5, 6, 7, 8, 9, and 10.

4. (Four Times Amended) A method of classifying a mycobacteria, comprising

providing a sample comprising a mycobacterial rpoB target nucleic acid from a mycobacteria;

determining the sequence of a segment of at least 50 contiguous bases from the target nucleic acid;

comparing the determined sequence to at least one sequence selected from the group consisting of SEQ ID NOS: [~~2-10~~] 2, 3, 4, 5, 6, 7, 8, 9, and 10; and

classifying the mycobacteria from the extent of similarity of the compared sequences.

6. (Four Times Amended) The method of claim 4, wherein the determined sequence is compared with at least nine sequences selected from the group consisting SEQ ID NOS: [~~2-10~~] 2, 3, 4, 5, 6, 7, 8, 9, and 10.

7. (Four Times Amended) A method of classifying a mycobacteria, comprising

_____providing a sample comprising a mycobacterial rpoB target nucleic acid;

_____determining the identity of one or more bases in the target sequence at one or more positions corresponding to one or more bases in a sequence selected from the group consisting of SEQ ID NOS: [~~2-10~~] 2, 3, 4, 5, 6, 7, 8, 9, and 10, wherein the one or more bases of the sequence selected from the group consisting of SEQ ID NOS. [~~2-10~~] 2, 3, 4, 5, 6, 7, 8, 9, and 10 differ from the corresponding one or more bases in SEQ ID NO. 1 when the sequences are maximally aligned, the identity of the one or more bases characterizing the species of mycobacteria that is present in the sample;

_____comparing the identified one or more bases in the target sequence to at least one sequence selected from the group consisting of SEQ ID NOS: [~~2-10~~] 2, 3, 4, 5, 6, 7, 8, 9, and 10; and

_____classifying the mycobacteria from the extent of similarity between the one or more bases identified in the target sequence and the corresponding one or more bases in the compared sequences.

8. (Four Times Amended) The method of claim 7, wherein the identity of at least 10 bases in the target nucleic acid at positions corresponding to the one or more bases in the sequence selected from the group consisting of SEQ ID NOS: [~~2-10~~] 2, 3, 4, 5, 6, 7, 8, 9, and 10 is determined.

9. (Five Times Amended) The method of claim 8, wherein the identity of at least 20 bases in the target sequence at positions corresponding to the one or more bases in the sequence selected from the group consisting of SEQ ID NOS: [~~2-10~~] 2, 3, 4, 5, 6, 7, 8, 9, and 10 is determined.

10. (Five Times Amended) The method of claim 9, further comprising comparing the at least 20 determined bases with at least 20 bases occupying corresponding positions in each of at least nine sequences selected from the group consisting of SEQ ID NOS: [~~2-10~~] 2, 3, 4, 5, 6, 7, 8, 9, and 10.

11. (Five Times amended) A [~~sequence-specific~~] polynucleotide probe or primer that hybridizes under stringent hybridization conditions to at least a contiguous segment of a mycobacterial rpoB sequence selected from the group consisting of SEQ ID NOS: [~~2-10~~] 2,

3, 4, 5, 6, 8, 9, and 10 or its complement without hybridizing to the *M. tuberculosis* sequence of SEQ ID NO: 1 or its complement, wherein the contiguous segment of the mycobacterial rpoB sequence includes at least about [20] 5 bases of [a] the mycobacterial rpoB sequence selected from the group consisting of SEQ ID NOS: [2-10] 2, 3, 4, 5, 6, 8, 9, and 10 which differ from the corresponding at least about 5 bases in SEQ ID NO: 1 when the sequences are maximally aligned; wherein said stringent hybridization conditions comprise 5 x SSPE and a temperature of 25-30°C.

12. (Three Times Amended) The [sequence-specific] polynucleotide of claim 11 that is a probe.

13. (Five Times Amended) The [sequence-specific] polynucleotide of claim 12, wherein a central position of the probe aligns with the one or more bases of a sequence selected from the group consisting of SEQ ID NOS: [2-10] 2, 3, 4, 5, 6, 8, 9, and 10 which differ from the corresponding one or more bases in SEQ ID NO: 1 when the sequences are maximally aligned.

15. (Five Times Amended) The [sequence-specific] polynucleotide of claim 14, wherein the 3' end of the primer aligns with the one or more bases of a sequence selected from the group consisting of SEQ ID NOS: [2-10] 2, 3, 4, 5, 6, 8, 9, and 10 which differ from the corresponding one or more bases in SEQ ID NO: 1 when the sequences are maximally aligned.

16. (Four Times Amended) The [sequence-specific] polynucleotide of claim 11 that hybridizes under stringent hybridization conditions to at least 100 contiguous bases of a mycobacterial rpoB sequence selected from the group consisting of SEQ ID NOS: [2-10] 2, 3, 4, 5, 6, 8, 9, and 10 or its complement without hybridizing to the M. tuberculosis sequence of SEQ ID NO: 1 or its complement.